REMARKS

Prior to the present amendment, claims 21 to 23, 26, 27 and 30 to 32 are pending, with claims 21 to 23 and 30 to 32 withdrawn from examination as allegedly drawn to a non-elected invention. Applicant respectfully draws the Examiner's attention to the fact that claim 21 has not been canceled but instead has been withdrawn from examination as allegedly drawn to a non-elected invention. Thus, claims 26 and 27 are presently under examination, with claims 21 to 23 and 30 to 32 pending but presently withdrawn from examination.

Applicant appreciates the Examiner's indication that claim 27 appears to be clear of the prior art and would be allowable if rewritten in independent form.

Regarding the amendments

Step (b) of claim 21 has been amended herein to conform to the language of claim 26. In addition, step (c) of claim 21 has been amended to more clearly indicate that the presence of a prostate neoplastic condition is indicated by a test expression level which is "significantly greater" than a control expression level. This amendment is supported throughout the specification, for example, at page 25, lines 10-14, which discloses that a significant test expression level was compared to a control expression level to indicate the presence of metastatic prostate cancer. Thus, the amendment is supported in the specification as filed and does not add new matter. Accordingly, Applicant respectfully requests that the Examiner enter the amendments.

Regarding the telephonic interview

In the telephonic interview on April 8, 2004, Applicant was informed that a claim directed to a PAMP polypeptide containing the amino acid sequence of SEQ ID NO: 2 would be allowed if rewritten in independent form, but that the broader claim, which encompasses amino acid substitutions relative to SEQ ID NO: 2, would be rejected as allegedly lacking enablement. The Examiner further proposed several amendments which would put the method of claim 21 in condition for allowance. Applicant declined to amend the claims at the time of the interview and requested a written action.

Regarding the rejection of claim 26 under 35 U.S.C. § 112, first paragraph

The rejection of claim 26 and corresponding objection to the specification under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement, respectfully are traversed. Claim 26 is directed to an isolated PAMP polypeptide containing an amino acid sequence having one or more conservative substitutions relative to SEQ ID NO: 2. The Office Action acknowledges that the specification enables a PAMP polypeptide having the amino acid sequence shown as SEQ ID NO: 2 but asserts that an amino acid sequence having one or more conservative substitutions relative to SEQ ID NO: 2 is not enabled. In this regard, the Office Action notes that the claimed PAMP polypeptide may have any number of conservative substitutions relative to SEQ ID NO: 2 and that overexpression of only a single species of PAMP polypeptide, i.e. SEQ ID NO: 2, has been demonstrated. The Office Action concludes that it is unpredictable whether a PAMP polypeptide having one or more conservative substitutions relative to SEQ ID NO: 2 will be overexpressed in prostate cancer

and that, therefore, one skilled in the art would not have been able to use the full scope of the invention.

Applicant submits that undue experimentation would not have been required to make and use the full scope of the invention, including polypeptides with one or more conservative substitutions relative to SEQ ID NO: 2. First, as previously acknowledged by the Examiner, the claimed invention has a well-established utility, that of preparing anti-PAMP antibodies, which can be used, for example, for identification of prostate tissue. As enablement for the claimed invention and as discussed further below, the specification provides guidance regarding how to make and use the claimed PAMP polypeptides as immunogens. In brief, the specification provides guidance, first, regarding making polypeptides related to SEQ ID NO: 2 by providing Figure 1, which discloses the amino acid sequence SEQ ID NO: 2 and corresponding nucleic acid sequence SEQ ID NO: 1, and in the specification, which teaches that PAMP polypeptides can be produced recombinantly (Figure 1 and page 22, lines 25-30). Secondly, guidance regarding use of a PAMP polypeptide as an immunogen for preparation of monoclonal and polyclonal antibodies is set forth at pages 21 to 23 of the specification (see, for example, page 21, line 31, to page 22, line 4; and page 22, line 25, to page 23, line 17). In regard to the use of anti-PAMP antibodies for identifying prostate tissue, the specification teaches that significant PAMP RNA expression was observed only in the prostate (page 9, lines 10-13). Thus, the specification provides guidance to the skilled person regarding the preparation of anti-PAMP antibodies and prostate-specific expression of PAMP transcripts. These results substantiate

that only routine methods would have been required for one skilled in the art to use a PAMP polypeptide having the amino acid sequence shown as SEQ ID NO: 2.

Applicant further submits that one skilled in the art would have been able to make and use a PAMP polypeptide having one or more conservative substitutions relative to SEQ ID NO: 2 irregardless of whether such a polypeptide is overexpressed in prostate cancer. In particular, one skilled in the art of immunology understands that an antibody prepared using a first polypeptide as an immunogen can cross-react against a second, highly related polypeptide. Thus, in the present case it is understood that an antibody prepared against a PAMP polypeptide having one or more conservative substitutions relative to SEQ ID NO: 2 can cross-react against SEQ ID NO: 2 itself. As evidence that antibody cross-reactivity was well known in the art, Applicant submits herewith as Exhibit A, Abbas et al., (Eds.), Cellular and Molecular Immunology, 2nd Ed., Chapter 3: *Antibodies and Antigens: Antibody Binding of Antigens*, page 47, (W.B. Saunders Co., Philadelphia, 1994). Abbas et al. indicate that an antibody binds only to a specific portion of a macromolecule called a **determinant** or **epitope** (page 47, second column first complete paragraph) and further state that:

> In proteins, epitopes formed by adjacent amino acid residues in the covalent sequence are called **linear determinants** (Fig. 3-9). It is estimated that, in a protein antigen, the size of the linear determinant that forms contacts with specific antibody is about six amino acids long. Linear determinants may be accessible to antibodies in the native folded protein if they appear on the surface or in a region of extended conformation. More often, linear determinants may be inaccessible in the native conformation and appear only when the protein is denatured. In contrast, **conformational**

> **determinants** are formed by amino acid residues from separated portions of the linear amino acid sequence that are spatially juxtaposed only upon folding.
> (page 47, second column, third complete paragraph)

The above makes clear that a linear determinant of 6 amino acid residues, which is conserved between SEQ ID NO: 2 and a PAMP polypeptide having one or more amino acid substitutions relative to SEQ ID NO: 2, can be sufficient for antibody reactivity. As further corroboration of Applicant's position, Applicant provides herewith as Exhibit B, *Antibodies To Cytokines & Related Molecules*, R&D Systems Catalog, pp. 141, 159, 164 (1999). As a few examples, multiple antibodies commercially available from R&D Systems exhibit cross-reactivity to species homologs or other highly related polypeptides: the anti-Bcl-X antibody #AF800 reacts with both human and murine Bcl-x (page 141); the anti-CPP32 polyclonal antibody #AF-506-NA reacts with full-length human CPP32 as well as 16, 18 and 20 kDa fragments of CPP32 (page 159), and the anti-cytochrome c antibody #MAB897 reacts with human as well as mouse cytochrome c (page 164). Thus, it is clear that antibody cross-reactivity between highly related polypeptides differing at one or more amino acid positions was well known in the art. These results substantiate that an antibody raised against a PAMP polypeptide having one or more conservative substitutions relative to SEQ ID NO: 2 also can react, and be useful for detecting, SEQ ID NO: 2 itself. In sum, irregardless of whether conservatively substituted PAMP polypeptides are overexpressed in prostate cancer tissue at the same level as the PAMP polypeptide having amino acid SEQ ID NO: 2, only routine work would have been required to practice the full scope of the invention.

In sum, we have argued, and the Examiner has previously acknowledged, that one utility for the claimed invention is to use a PAMP polypeptide as an immunogen for the preparation of antibodies for detecting overexpression of SEQ ID NO: 2. Applicant maintains that one skilled in the art would have been able to use an antibody against a PAMP polypeptide having one or more conservative substitutions relative to SEQ ID NO: 2 in essentially the same manner as one skilled in the art would use a PAMP polypeptide having the amino acid sequence shown as SEQ ID NO: 2. In view of the above, Applicant respectfully requests that the Examiner reconsider and remove the rejection of claim 26 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement.

Regarding method claim 21

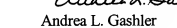
In the recent telephonic interview, Applicant declined to amend method claim 21 to indicate that the recited "sample" is a "sample of prostate tissue." In this regard, Applicant respectfully draws the Examiner's attention to the Declaration under 35 U.S.C. § 1.132 by Dr. Biaoyang Lin, filed on October 31, 2002. As indicated in paragraph 5 of the Declaration and shown in Figure 1 attached thereto, PAMP polypeptide was detected in a serum sample from a prostate cancer patient, evidencing that PAMP polypeptide expression can be detected in samples other than tissue samples. In view of the above, Applicant respectfully submits that claim 21 is patentable as written.

CONCLUSION

In light of the amendments and remarks herein, Applicant submits that the claims are now in condition for allowance and respectfully requests a notice to this effect. Should the Examiner have any questions, she is invited to call the undersigned agent or Cathryn Campbell.

Respectfully submitted,

MCDERMOTT WILL & EMERY LLP



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